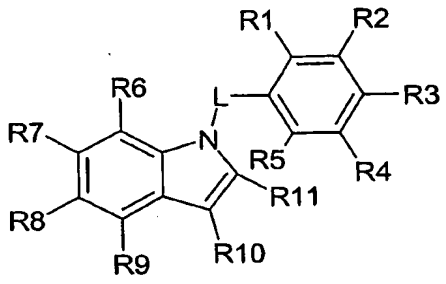
CLAIMS

What is claimed is:

1. A compound of the formula



or a pharmaceutically acceptable salt thereof,

wherein L is $-C(=O)-$ or $-CH_2-$;

R1, R2, R4, R5, R6, R7, and R9 are independently H; OH; halo (e.g., F, Cl, Br, I); C_{1-6} alkyl; C_{1-6} haloalkyl (e.g., CHF_2, CF_3); C_{1-6} alkoxy optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably $-OCF_3$, $-OCHF_2$;

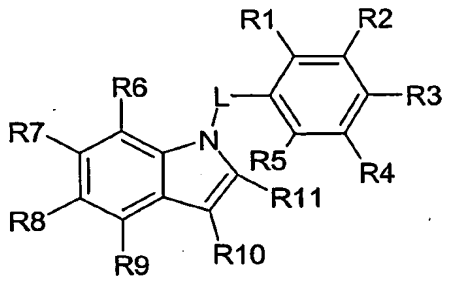
R3 is selected from the group consisting of $-CHF_2$, $-CF_3$, $-OCF_3$, $-OCHF_2$, and preferably $-CF_3$ or $-OCF_3$;

R8 is H; halo (e.g., F, Cl, Br, I); C_{1-6} alkyl (e.g., preferably methyl, ethyl, propyl, isopropyl, or $-C(CH_3)_3$); C_{1-6} haloalkyl (e.g., CHF_2, CF_3); or C_{2-6} alkoxy optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably ethoxy, propyloxy and isopropyloxy;

R10 is $-R^L-COOH$, wherein R^L is selected from C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl, preferably $-CH_2-$; and

R11 is a C_{1-3} alkyl (e.g., methyl, ethyl, propyl, isopropyl), preferably methyl.

2. A compound of the formula



or a pharmaceutically acceptable salt thereof,

wherein L is –C(=O)–;

R1, R2, R4, R5, R6, R7, and R9 are independently H; halo (e.g., F, Cl, Br, I); C_{1-3} alkyl; C_{1-3} haloalkyl (e.g., CHF_2, CF_3); or C_{1-3} alkoxy optionally substituted with 1, 2, 3, or 4 halo (e.g., F, Cl, Br, I), preferably -OCF_3, -$OCHF_2$; Preferably, R1, R2, R4, R5, R6, R7, and R9 are independently H or halo or methyl;

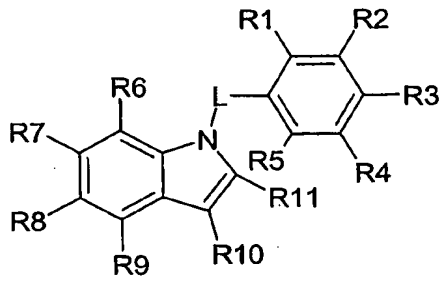
R3 is–OCF_3;

R8 is H; F, Cl or Br; C_{1-6} alkyl (e.g., preferably methyl, ethyl, propyl, isopropyl, or –$C(CH_3)_3$); C_{1-6} haloalkyl (e.g., CHF_2, CF_3); or C_{2-6} alkoxy optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably ethoxy, propyloxy and isopropyloxy;

R10 is –CH_2COOH; and

R11 is a C_{1-3} alkyl (e.g., methyl, ethyl, propyl, isopropyl), preferably methyl.

3. A compound of the formula



wherein L is $-CH_2-$;

R1, R2, R4, R5, R6, R7, and R9 are independently H; OH; halo (e.g., F, Cl, Br, I); C_{1-6} alkyl; C_{1-6} haloalkyl (e.g., CHF_2, CF_3); C_{1-6} alkoxy optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably $-OCF_3$, $-OCHF_2$;

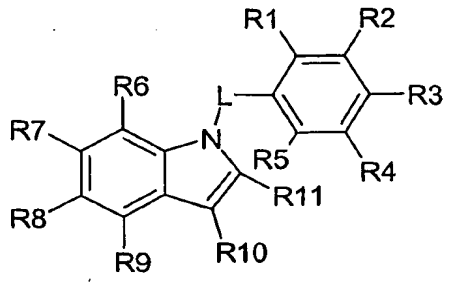
R3 is $-CF_3$;

R8 is H; halo (e.g., F, Cl, Br, I); C_{1-6} alkyl (e.g., preferably methyl, ethyl, propyl, isopropyl, or $-C(CH_3)_3$); C_{1-6} haloalkyl (e.g., CHF_2, CF_3); or C_{2-6} alkoxy optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably ethoxy, propyloxy and isopropyloxy; Preferably R8 is C_{1-4} alkyl (e.g., methyl, ethyl, propyl, isopropyl, or $-C(CH_3)_3$);

R10 is $-CH_2COOH$; and

R11 is a C_{1-3} alkyl (e.g., methyl, ethyl, propyl, isopropyl), preferably methyl.

4. A compound of the formula



or a pharmaceutically acceptable salt thereof,

wherein L is $-CH_2-$ or $-CH(C_{1-6}$ alkyl)–, and preferably $-CH_2-$;

R1, R2, R4, R5, R6, R7, R9 and R10 are independently H; OH; halo (e.g., F, Cl, Br, I); C_{1-6} alkyl; C_{1-6} haloalkyl (e.g., CHF_2, CF_3); C_{1-6} alkoxy optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably $-OCF_3$, $-OCHF_2$; or C_{1-6} alkyl-S– optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably $-SCF_3$;

R3 is selected from the group consisting of C_{1-3} haloalkyl (e.g., $-CHF_2$, $-CF_3$), $-SCF_3$, C_{1-3} alkoxy, or C_{1-3} haloalkoxy (e.g., $-OCF_3$, $-OCHF_2$), wherein optionally R_3 forms a 5 or 6-membered heterocycle with the adjacent R2 or R4 group;

R8 is H; halo (e.g., F, Cl, Br, I); C_{1-6} alkyl; C_{1-6} haloalkyl (e.g., CHF_2, CF_3); C_{1-6} alkoxy optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably ethoxy, propyloxy and isopropyloxy; C_{1-6} alkyl–S– optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I); or $-S(O)_2-(C_{1-6}$ alkyl); $-NO_2$;

R11 is selected from the group consisting of $-R^L-C(=O)R_{42}$, $-R^L-C(=S)R_{42}$, $-R^L-C(=O)S-R_{43}$, $-R^L-C(=O)N(R_{52})(R_{53})$, $-S(O)_2-(C_{1-6}$ alkyl); $-R^L-$phosphono, and $-R^L-$tetrazolyl;

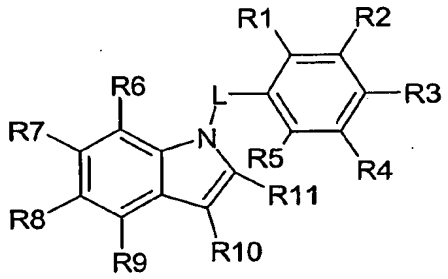
R^L is selected from a bond, C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl, preferably a bond or C_1 alkyl;

R_{42} is selected from H, -OH, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, and C_{1-6} alkylthiol, wherein R_{42} is optionally substituted with from one to three substituents independently selected from halo, N_3, nitro, hydroxy, thiol, CN and C_{1-6} alkyl;

R_{43} is H, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, wherein R_{43} is optionally substituted with from one to three substituents independently selected from halo, N_3, nitro, hydroxy, thiol, CN and C_{1-6} alkyl; and

R_{52} and R_{53} are independently H, OH (R_{52} and R_{53} are not both OH), C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{1-10} alkoxy, C_{1-10} alkylthiol, C_{2-10} alkenyloxy, C_{2-10} alkynyloxy, C_{1-10} haloalkyl, C_{2-6} hydroxyalkyl, C_{1-6} alkyl-O-C_{1-6} alkyl–, or R_{52} and R_{53} together with the nitrogen atom to which they are both linked form a 3, 4, 5 or 6-membered heterocycle (e.g., piperidinyl, pyrrolidinyl, and morpholinyl), wherein R_{52} and R_{53} each is optionally substituted with 1-3 substituents wherein each substituent is independently halo, N_3, nitro, hydroxy, thiol, CN, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, $-C(=O)N(R_{54})(R_{55})$, $R_{44}C(=O)-$ or $-N(R_{54})(R_{55})$, wherein R_{54} and R_{55} are independently H, OH or C_{1-4} alkyl, and wherein R_{44} is H or C_{1-4} alkyl.

5. A compound of the formula



or a pharmaceutically acceptable salt thereof,

wherein L is $-CH_2-$;

R1, R2, R4, R5, R6, R7, R9 and R10 are independently H; OH; halo (e.g., F, Cl, Br, I); C_{1-6} alkyl; C_{1-6} haloalkyl (e.g., CHF_2, CF_3); C_{1-6} alkoxy optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably -OCF_3, -$OCHF_2$; or C_{1-6} alkyl-S– optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably -SCF_3;

R3 is selected from the group consisting of $-CHF_2$, $-CF_3$, $-OCF_3$, or $-OCHF_2$;

R8 is H; halo (e.g., F, Cl, Br, I); C_{1-6} alkyl; C_{1-6} haloalkyl (e.g., CHF_2, CF_3); C_{1-6} alkoxy

optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I), preferably ethoxy, propyloxy and isopropyloxy; C_{1-6} alkyl–S– optionally substituted with 1, 2, 3, and 4-6 halo (e.g., F, Cl, Br, I); or $-S(O)_2-(C_{1-6}$ alkyl); $-NO_2$;

R11 is selected from the group consisting of $-R^L-COOH$; and

R^L is selected from a bond, C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl, preferably a bond.

6. A method of reducing $A\beta_{42}$ production or secretion in a mammalian cell, comprising administering to the cell a compound according to anyone of Claims 1-5.

7. Use of the compound according to anyone of Claims 1-5 in the manufacture of a medicament useful in treating a disease amenable to reduction of cellular $A\beta_{42}$ production or secretion.

8. The use of Claim 7, wherein said medicament is used in treating a neurodegenerative disorder selected from the group consisting of dementia, Alzheimer's disease, MCI, Parkinson's disease, Down's syndrome, and tauopathies (corticobasal degeneration, and progressive supranuclear palsy).

9. The use of Claim 7, wherein said medicament is used in treating inclusion body myositis.